

- 3
Cont
- (a) the sequence shown in SEQ ID NO:1,
(b) a part of SEQ ID NO:1 which encodes nucleotide 1783-2142 and encodes the mature protein,
(c) a nucleotide sequence which encodes the amino acid sequence according to SEQ ID NO: 2,
(d) a nucleotide sequence which encodes a portion of the amino acid sequence according to SEQ ID NO:2, wherein said portion is the mature protein.--

REMARKS

Claims 6, 9, 11, 13, 16, 20-22 and 27-29 are pending in this application. By this Amendment, claims 11 and 27 are amended and new claims 28 and 29 are added.

START OF MATURE PROTEIN

In principal, the Examiner is correct that the mature protein begins at nucleotide 1783. Claim 11 b) has been corrected accordingly so that it again defines a mature protein beginning at nucleotide 1783.

Claim Rejections - 35 U.S.C. § 112, second paragraph

Claims 11 and 27 are rejected as indefinite. The Examiner indicates that the rejection of claim 11 would be overcome by deleting the terminology "and which has essentially the same osteoinductive activity of the protein" from the claim. Applicants

have amended claim 11 accordingly. Applicants have also corrected the typographical error of --dimer-- in claim 27.

For at least these reasons, Applicants respectfully submit that the rejections under 35 U.S.C. § 112, second paragraph, are overcome. Reconsideration and withdrawal thereof are respectfully requested.

With regard to claim 11 e), Applicants have followed the suggestion of the Examiner to delete the supplementary term "and which has essentially the same osteoinductive activity of the protein".

The Examiner is right that the protein sequence SEQ ID NO. 13 corresponds with the mouse GDF-5 sequence of Lee. However the human DNA sequence deviates from the mouse sequence. Thus, to further clarify the present invention, claim 11, part (e) has been amended to define *"a part of SEQ ID NO. 1 which encodes the amino acid sequence according to SEQ ID NO. 13"*.

Section 102/103 Rejections

Claims 11 and 27 are rejected under 35 U.S.C. 102 as being anticipated by Lee et al. (U.S. Patent No. 5,801,014). Similarly, claims 9, 11, 13, 16, 20 and 24-27 are rejected under 35 U.S.C. 103(a) as being obvious over Lee alone or in view of Opperman et al. (U.S. Patent No. 5,266,683). These rejections are traversed as they may apply to the amended claims.

This rejection is based on section e) of claim 11, which reads "e) a nucleotide sequence which encodes a portion of the amino acid sequence according to SEQ ID

NO:2, wherein said portion comprises the seven cysteine region as shown in SEQ ID NO: 13 and which has essentially the same osteoinductive activity of the protein."

The Examiner rejects all claims which comprise a Lee sequence and/or pharmaceutical compounds thereof. He argues, however, that Lee does not comprise pharmaceutical compounds, but asserts that it is obvious from Oppermann that BMPs can be inserted as a pharmaceutical compound in connection with a matrix.

As claim 11 e) has however been amended and the Lee sequence is not comprised, the combination with Oppermann no longer reaches the presently claimed invention.

Applicants also respectfully note that neither of Lee or Oppermann protect the angiogenesis. Thus, the new present claim directed to a pharmaceutical compound for angiogenesis would not have been obvious thereover. Lee mentions GDF-5 primarily in connection with "skeletal tissue (cartilage/bone)" or "uterus".

Double Patenting

The Office Action rejects claims 6, 9, 11, 13, 16, 20, 21-22 and 24-27 under the judicially created doctrine of obviousness type double patenting as being obvious over claims 1-6 in U.S. Patent No. 6,120,760 to Hotten et al.

However, Applicants respectfully note that Hotten et al. was filed August 12, 1994 while the present application is a divisional of Application Serial Number 08/288,505 filed August 10, 1994. Thus, Hotten et al., should not be prior art to the present application.

Conclusion

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300.

Respectfully submitted,



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Attachment: Amended Claims 11 and 27 Marked-Up to Show Changes

Amended Claims 11 and 27 Marked-Up to Show Changes

11. (Amended) An isolated protein of the TGF- β family encoded by an isolated DNA molecule which comprises a sequence selected from the group consisting of:

- a) the sequence shown in SEQ ID NO:1,
- b) a part of SEQ ID NO:1 which encodes nucleotide --1783-- [1782]-2142 and encodes the mature protein,
- c) a nucleotide sequence which encodes the amino acid sequence according to SEQ ID NO: 2,
- d) a nucleotide sequence which encodes a portion of the amino acid sequence according to SEQ ID NO:2, wherein said portion is the mature protein, and
- e) a part of SEQ ID NO. 1 which encodes the amino acid sequence according to SEQ ID NO:13.

27. (Amended) A protein according to claim 11, wherein the protein is a dimer [dimmer].